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NEWS 8 AUG 18 FROSTI and KOSMET enhanced with Simultaneous Left and Right
Truncation
NEWS 9 AUG 18 Simultaneous left and right truncation added to ANABSTR
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FILE COVERS 1907 - 14 Oct 2003 VOL 139 ISS 16
FILE LAST UPDATED: 13 Oct 2003 (20031013/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s microsphere and biodegradable and insulin

11605 MICROSPHERE
18947 MICROSPHERES
21160 MICROSPHERE
(MICROSPHERE OR MICROSPHERES)
23930 BIODEGRADABLE
19 BIODEGRADABLES
23942 BIODEGRADABLE
(BIODEGRADABLE OR BIODEGRADABLES)
155313 INSULIN
5150 INSULINS
155389 INSULIN
(INSULIN OR INSULINS)

L1 59 MICROSPHERE AND BIODEGRADABLE AND INSULIN

=> s L1 and polylactic

3314 POLYLACTIC

L2 5 L1 AND POLYLACTIC

=> d L2 1-5 ibib abs hitrn

L2 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:762783 CAPLUS

DOCUMENT NUMBER: 135:322723

TITLE: Proteins deposited onto sparingly soluble biocompatible particles for controlled protein release into a biological environment from a polymer matrix

INVENTOR(S): Shih, Chung; Zentner, Gaylen; Piao, Ai-Zhi

PATENT ASSIGNEE(S): Macromed, Inc., USA

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001076558	A1	20011018	WO 2001-US11217	20010406
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002015737 A1 20020207 US 2001-827100 20010405
 EP 1267838 A1 20030102 EP 2001-924765 20010406

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2001010319 A 20030729 BR 2001-10319 20010406
 NZ 521994 A 20030829 NZ 2001-521994 20010406

PRIORITY APPLN. INFO.: US 2000-195700P P 20000407
 US 2001-827100 A 20010405
 WO 2001-US11217 W 20010406

AB The present invention relates to compns. and methods for the modulated release of one or more proteins or peptides. The compn. is comprised of a biocompatible polymeric matrix, a protein and/or peptide, and a sparingly water-sol. or essentially insol. particle. The protein is deposited by adsorption or some other mechanism onto the sparingly water-sol. biocompatible particle wherein the protein-particle combination is dispersed within the polymeric matrix. The deposition of the protein onto the particle acts to modulate the release of the protein or peptide from dosage forms including long-acting dosage systems. To a soln. of 5 mg/3mL human growth hormone was added to 100 mg of zinc carbonate and the suspension was allowed to stand in a refrigerator at 4.degree. for 16 h. HPLC anal. showed that the mass balance recovery of hGH, after removal of zinc using EDTA, was quant. In vivo pharmacokinetics of hGH sustained-release formulation was studied in rats.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:300548 CAPLUS
 DOCUMENT NUMBER: 134:316141

TITLE: Injection vehicle for polymer-based formulations
 INVENTOR(S): Cleland, Jeffrey L.; Lam, Xanthe M.; Okumu, Franklin
 PATENT ASSIGNEE(S): Genetech, Inc., USA
 SOURCE: PCT Int. Appl., 26 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028591	A2	20010426	WO 2000-US26258	20001016
WO 2001028591	A3	20020307		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1220690 A2 20020710 EP 2000-971986 20001016

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: US 1999-159739P P 19991015
 WO 2000-US26258 W 20001016

AB The invention provides injection vehicles suitable for administering particulate suspensions, such as polymer-based formulations, as well as assocd. pharmaceutical formulations, articles of manuf., and kits. Other aspects of the invention included methods for producing and administering

pharmaceutical formulations. The injection vehicles of the invention are superior to conventional injection vehicles in that they include a pseudoplastic compn. that improves injectability, which facilitates delivery of the desired dose. The injection vehicles of the invention also allow the use of smaller-bore needles than are usually necessary to inject polymer-based formulations, reducing the pain assocd. with injection of such formulations. Syringeability of **microspheres** contg. proteins such as anti-rhGH Fab polymer-based formulations or VEGF, or other proteins and contg. Na hyaluronate was studied.

L2 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:513547 CAPLUS
DOCUMENT NUMBER: 133:125280
TITLE: Compositions and methods for controlled delivery of virus vectors
INVENTOR(S): Levy, Robert J.; Jones, Peter L.
PATENT ASSIGNEE(S): Children's Hospital of Philadelphia, USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043044	A1	20000727	WO 2000-US1193	20000119
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-116405P P 19990119

AB The invention relates to compns. and methods for delivering a virus vector to an animal. The compns. include compns. which comprise a matrix having a virus vector bound at the exterior surface thereof in a physiol. reversible manner. The invention also includes methods of making such compns., including particles, devices, bulk materials, and other objects which comprise, consist of, or are coated with such compns. Methods of delivering a virus vector to an animal tissue are also described.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:282075 CAPLUS
DOCUMENT NUMBER: 130:316644
TITLE: Encapsulation method using **biodegradable** polymers
INVENTOR(S): Laakso, Timo; Reslow, Mats
PATENT ASSIGNEE(S): Bioglan Therapeutics AB, Swed.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920253	A1	19990429	WO 1998-SE1717	19980924

W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
 CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR,
 HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
 LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
 SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

SE 9703874	A	19990424	SE 1997-3874	19971023
SE 512663	C2	20000417		
CA 2306824	AA	19990429	CA 1998-2306824	19980924
AU 9894670	A1	19990510	AU 1998-94670	19980924
AU 732891	B2	20010503		
EP 1033973	A1	20000913	EP 1998-948005	19980924
EP 1033973	B1	20030917		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
 JP 2001520186 T2 20011030 JP 2000-516653 19980924
 ZA 9809199 A 19990415 ZA 1998-9199 19981008
 NO 2000002039 A 20000613 NO 2000-2039 20000418

PRIORITY APPLN. INFO.:

SE 1997-3874 A 19971023
 WO 1998-SE1717 W 19980924

AB This invention provides a novel method of encapsulating an active substance in a **biodegradable** polymer, which comprises: (a) dissolving the **biodegradable** polymer in an org. solvent; (b) dispersing the active substance in the org. soln. obtained in step (a) to provide a dispersion with the active substance as the inner phase thereof, or alternatively, emulsifying the active substance, dissolved in water or other aq. solvent, in the org. soln. obtained in step (a) to provide an emulsion with the active substance as the inner aq. phase; and (c) subjecting the dispersion or emulsion to an encapsulation operation with an aq. polyethylene glycol soln. as a continuous phase to provide micro- or nanoparticles having the active substance encapsulated therein. A soln. of glycolide-lactide copolymer was prepd. by dissolving the polymer in EtOAc, then bovine serum albumin dissolved in a phosphate buffer was added to the polymer soln. The obtained homogeneous dispersion was slowly injected into the soln. of polyethylene glycol with stirring. Deionized water was added to reduce the viscosity of the suspension for filtration using a Millipore membrane. The filtrate was washed with water and dried to obtain spherical microparticles.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:149502 CAPLUS

DOCUMENT NUMBER: 128:184709

TITLE: **Microspheres** comprising a polymer and a drug dispersed within it

INVENTOR(S): Mathiowitz, Edith; Mullon, Claudy J. P.; Domb, Abraham J.; Langer, Robert S.

PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA

SOURCE: U.S., 9 pp., Cont. of U. S. Ser. No. 304,702, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5718921	A	19980217	US 1996-691874	19960802
PRIORITY APPLN. INFO.:			US 1987-25409	19870313
			US 1989-304702	19890201

AB A method for prepn. of **biodegradable** polymeric drug delivery devices using relatively low temps. and non-aq. solns. which is particularly useful with polyanhydrides, thermolabile drugs, and in forming multi-layered devices. In a first embodiment, the polymer is dissolved in a volatile org. solvent, the drug is dispersed or dissolved in the polymer soln., the mixt. is suspended in an org. oil, and the org. solvent is extd. into the oil, creating **microspheres**. The preferred polymers are polyanhydrides since they are **biodegradable** and have been proven to be useful in vivo. In a second embodiment, the polymer is dissolved in org. solvent with or without the drug, and the mixt. is suspended in glycerol. The suspension is frozen and the org. solvent slowly evapd. Using these embodiments, alone or in combination with other methods including the "hot melt" technique, multi-walled **microspheres** having each wall degrading at a different rate or contg. different drugs can be manufd. **Microspheres** were prepd. from p-carboxyphenoxy propane-sebasic acid copolymer, silicone oil, and **insulin** according to above method. In vitro and in vivo release of **insulin** was studied.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s L1 and bicarbonate
43282 BICARBONATE
6388 BICARBONATES
47760 BICARBONATE
(BICARBONATE OR BICARBONATES)
L3 3 L1 AND BICARBONATE

=> d L3 1-3 ibib abs hitrn

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:780648 CAPLUS
DOCUMENT NUMBER: 135:335147
TITLE: Polymer-based injectable sustained release
pharmaceutical compositions for peptide and protein
drugs
INVENTOR(S): Lee, Hee-yong; Lee, Hye-suk; Kim, Jung-soo; Kim,
Sang-beom; Lee, Ji-suk; Choi, Ho-il; Chang, Seung-gu
PATENT ASSIGNEE(S): Peptron Inc., S. Korea
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078687	A1	20011025	WO 2001-KR462	20010322
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1187602	A1	20020320	EP 2001-917893	20010322
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
US 2003026844	A1	20030206	US 2002-18870	20020418
PRIORITY APPLN. INFO.:			KR 2000-20484	A 20000418

KR 2000-49344 A 20000824
WO 2001-KR462 W 20010322

AB Controlled and sustained release injectable pharmaceutical compns. for a biopharmaceutical, such as peptides and proteins are described. Processes for prepn. of an injectable sustained release compn. comprises (i) a step of prepg. **biodegradable** porous **microspheres** having accessible ionic functional groups, (ii) a step of encapsulating a biopharmaceutical into the **microspheres** through ionic interaction by suspending or equilibrating the **microspheres** in a soln. contg. the biopharmaceutical, and (iii) a step of recovering and freeze-drying the biopharmaceutical-incorporated **microspheres**. For example, **microspheres** were prepd. by water/oil/water double emulsion solvent evapn. method using a hydrophilic 50:50 PLGA polymer (RG 502H), which contains free carboxy end groups. Deionized water (800 mL) was added to 1 g of PLGA polymer dissolved in 2 mL of methylene chloride and emulsified by sonication for 30 s using a probe type ultrasonic generator. This primary emulsion was dispersed into 200 mL of deionized water contg. 0.5% polyvinyl alc. (wt./vol.) in a vessel which connected to a const. temp. controller and mixed well by stirring for 15 min at 2500 rpm, 25.degree. using a mixer. After mixing for another 15 min at 1500 rpm, 25.degree., temp. of continuous phase was increased to 40.degree. to evap. methylene chloride. After 1 h stirring at 40.degree., 1500 rpm, temp. was decreased to 25.degree.. The hardened **microspheres** were collected by centrifugation and washed twice with 200 mL of deionized water, and then freeze-dried. The **microspheres** obtained were used for incorporation of protein drugs, i.e., ovalbumin, bovine serum albumin, human growth hormone, RNase A, or lysozyme through ionic interaction by simply soaking and equilibrating the **microspheres** into a buffer soln. having an appropriate concn. of protein.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:880988 CAPLUS

DOCUMENT NUMBER: 134:46791

TITLE: Modified **biodegradable** polyester **microspheres** for stabilizing and improving the release profile of encapsulated drugs

INVENTOR(S): Bailey, Leonard C.; Shao, Pushpa G.

PATENT ASSIGNEE(S): Rutgers, the State University, USA

SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000074709	A2	20001214	WO 2000-US14875	20000530
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 1999-137289P P 19990603

AB Modified **biodegradable microspheres** for encapsulation of a peptide or protein drug, e.g. **insulin**, made up of a **biodegradable** polymer and a basic excipient are provided. The **biodegradable** polymer comprises poly(L-lactic acid) or a copolymer

of L-lactic acid with D-lactic acid or glycolic acid, and the basic excipient comprises a **bicarbonate**. Also provided are methods of improving the release profile of a drug and delivering a drug to a patient via encapsulation of the drug within these modified **biodegradable microspheres**. For example, porcine **insulin microspheres** with a theor. **insulin** loading of approx. 3.2% contg. NaHCO₃ (theor. loading level of 7.7%) were prepd. using Resomer RG 504 by an emulsion solvent evapn. method.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:742436 CAPLUS

DOCUMENT NUMBER: 132:83486

TITLE: Stabilization of pH-induced degradation of porcine **insulin in biodegradable polyester microspheres**

AUTHOR(S): Shao, Pushpa G.; Bailey, Leonard C.

CORPORATE SOURCE: Warner-Lambert Research Division, Morris Plains, NJ, USA

SOURCE: Pharmaceutical Development and Technology (1999), 4(4), 633-642

CODEN: PDTEFS; ISSN: 1083-7450

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose of this research project was to stabilize the pH-induced degrdn. of porcine **insulin** encapsulated within **biodegradable polyester microspheres** through the incorporation of a basic additive. **Insulin microspheres** fabricated using Poly(L-lactide) (L-PLA) and Poly(DL-lactide-co-glycolide) (50:50 DL-PLGA) were subjected to in vitro release studies and the stability of unreleased **insulin** encapsulated within **microspheres** was investigated. The intramicrosphere pH was estd. by encapsulating acid-base indicators covering a wide pH transition range within 50:50 DL-PLGA **microspheres**. Finally, a basic excipient sodium **bicarbonate** was incorporated in 50:50 DL-PLGA **microspheres** to minimize acid-induced **insulin** degrdn. The in vitro release was slow and incomplete (<30% in 30 days). Extn. and analyses of the unreleased **insulin** within the **microspheres** revealed that an av. of .apprx.11% remained intact. The degrdn. products obsd. consisted of .apprx.15% of three distinct deamidated hydrolysis products including A-21 Desamido **insulin**, .apprx.22% Covalent **Insulin** Dimer and trace amts. of High Mol. Wt. Transformation Products. Comparison of the degrdn. profile of unreleased **insulin** contained in various **microsphere** formulations with the in vitro release kinetics indicated that an increase in covalent dimer formation within the **microspheres** prior to release is assocd. with a decrease in the cumulative percent **insulin** released during a 30-day incubation period. In an attempt to correlate **insulin** degrdn. with the drop in intra-**microsphere** pH due to polymer hydrolysis, it was detd. that the pH within a degrading **microsphere** reaches a value of .apprx.1.8 after 4 wk. The incorporation of a basic excipient, sodium **bicarbonate**, in 50:50 DL-PLGA **microspheres** resulted in an improved in vitro release profile (cumulative release .apprx.47.3% in 30 days) as well as a significant redn. in covalent dimerization of the unreleased **insulin** to barely detectable levels. The low pH microenvironment within a degrading **microsphere** is one of the major factors leading to protein instability, and the degrdn. of proteins encapsulated within polyester **microspheres** can be minimized by the incorporation of a basic excipient.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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	ENTRY	SESSION
CA SUBSCRIBER PRICE	-5.21	-5.21

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 10, 2003 (20031010/UP).